

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of making an array comprising:
applying building block molecules to a solid support in a plurality of regions, each region:
 - comprising 2, 3, 4, 5, or 6 different building block molecules;
 - being a contiguous portion of the surface of the solid support with the different building block molecules distributed randomly ~~and evenly~~ throughout the contiguous region; and
 - having the shape of a spot;independently reversibly immobilizing the different block molecules on the solid support in the regions;
 - building block molecules being independently reversibly immobilized by a readily reversible covalent bond, interaction between ions, hydrogen bonding, or van der Waals interactions;
 - each region comprising building blocks immobilized by van der Waals interactions comprising a lawn of moieties that can engage in van der Waals interactions, the lawn being covalently coupled to the solid support;producing an array comprising a candidate artificial receptor, a lead artificial receptor, a working artificial receptor, or a combination thereof;
wherein:
 - a first region comprises a first combination of block molecules and a second region comprises a second combination of block molecules;
 - at least one of the block molecules is naïve with respect to a test ligand; and
 - each building block molecule comprises a framework and n recognition elements and is independently of the formula:
$$\text{framework}-(\text{recognition element})_n$$in which:

$n=1, 2, \text{ or } 3$; each recognition element is independently covalently coupled to the framework; and the framework comprises a functional group effective for covalent coupling to a linker, a structural moiety or functional group effective for reversible coupling to a support, or a combination thereof;

the framework is alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl; substituted with 1 to 4 functional groups;

the functional groups independently being carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol;

each recognition element is independently a 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl moiety; substituted with a group with a property of positive charge, negative charge, acid, base, electron acceptor, electron donor, hydrogen bond donor, hydrogen bond acceptor, free electron pair, π electrons, charge polarization, hydrophilicity, or hydrophobicity; and

when the building block molecule comprises an amino acid derivative, wherein amino acid derivatives are defined as a core feature having the chemical structure $-\text{NH}-\text{C}-\text{C}(\text{O})-$, the building block molecule comprises a single amino acid derivative and the framework is the amino acid derivative.

2. (Currently amended) The method of claim 1, further comprising:
mixing the different block molecules; and
wherein applying comprises applying ~~employing~~ the mixture of building block molecules to the solid support in at least one of the regions.
3. (Previously presented) The method of claim 1, wherein applying comprises piezoelectric spotting, pin spotting, electromagnetic spotting, or photolithography.
4. (Original) The method of claim 1, wherein the solid support comprises a glass plate or microscope slide.
- 5-7. (canceled)

8. (Currently Amended) A method of making an artificial receptor, the method comprising:

applying building block molecules to a region on a solid support, the region:

comprising 2, 3, 4, 5, or 6 different building block molecules; and

being a contiguous portion of the surface of the solid support with the different building block molecules distributed randomly and evenly throughout the contiguous region;

independently reversibly immobilizing the different building block molecules on the support in the region;

building block molecules being independently reversibly immobilized by a readily reversible covalent bond, interaction between ions, hydrogen bonding, or van der Waals interactions;

each region comprising building blocks immobilized by van der Waals interactions comprising a lawn of moieties that can engage in van der Waals interactions, the lawn being covalently coupled to the solid support;

wherein:

2 or more of the different building block molecules together forming a candidate artificial receptor, a lead artificial receptor, a working artificial receptor, or a combination thereof;

at least one of the building block molecules is naïve with respect to a test ligand.

each building block molecule comprises a framework and n recognition elements and is independently of the formula:

$$\text{framework-(recognition element)}_n$$

in which:

n=1, 2, or 3; each recognition element is independently covalently coupled to the framework; and the framework comprises a functional group effective for covalent coupling to a linker, a structural moiety or functional group effective for reversible coupling to a support, or a combination thereof;

the framework is alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl; substituted with 1 to 4 functional groups;

the functional groups independently being carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol;

each recognition element is independently a 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl moiety; substituted with a group with a property of positive charge, negative charge, acid, base, electron acceptor, electron donor, hydrogen bond donor, hydrogen bond acceptor, free electron pair, π electrons, charge polarization, hydrophilicity, or hydrophobicity; and

when the building block molecule comprises an amino acid derivative, wherein amino acid derivatives are defined as a core feature having the chemical structure $-\text{NH}-\text{C}-\text{C}(\text{O})-$, the building block molecule comprises a single amino acid derivative and the framework is the amino acid derivative.

9. (Currently Amended) The method of claim 8, wherein the region is in the shape of a spot-region.

10-66. (Cancelled).

67. (Currently amended) The method of claim 8, further comprising:
mixing the different block molecules; and
wherein applying comprises applying ~~employing~~ the mixture of building block molecules to the solid support in the region.

68. (Previously presented) The method of claim 8, wherein applying comprises piezoelectric spotting, pin spotting, electromagnetic spotting, or photolithography.

69. (Previously presented) The method of claim 8, wherein the solid support comprises a glass plate or microscope slide.

70. (Currently amended) The method of claim 1, wherein each recognition element is independently unsubstituted or substituted with a moiety selected from the group consisting of amine, quaternary ammonium, carboxylate, phenol, phosphate, phosphonate, phosphinate,

sulphate, sulphonate, thiocarboxylate, hydroxamic acid, sulfoxide, betaine, amine oxide, amide, carboxyl, alcohol, ether, thiol, thioether, ester, thio ester, borane, borate, metal complex, alkyl, alkene, alkyne, aromatic moiety, and plurality thereof.

71. (Previously presented) The method of claim 1, wherein a recognition element is substituted with or to form:

protonated phosphate, protonated phosphonate, protonated phosphinate, protonated sulphate, or protonated sulphinate;

alkyl amine, alkyl diamine, heteroalkyl amine, aryl amine, heteroaryl amine, aryl alkyl amine, heterocyclic amine, amidine, hydrazine, urea, trimethyl alkyl quaternary ammonium, dimethyl ethyl alkyl quaternary ammonium, dimethyl alkyl quaternary ammonium, aryl alkyl quaternary ammonium, or pyridinium quaternary ammonium;

alkyl carboxylate, aryl carboxylate, aryl alkyl carboxylate, or thiocarboxylate;

phosphonate or phosphinate;

primary alcohol, secondary alcohol, tertiary alcohol, or aromatic alcohol;

lower alkyl, substituted alkyl, cycloalkyl, aryl alkyl, heteroaryl alkyl, lower alkene, aryl alkene, unsubstituted aryl, heteroaryl, substituted aryl, aryl alkyl, heteroaryl alkyl, alkyl substituted aryl, or polyaromatic hydrocarbon; or

a plurality thereof.

72. (Previously presented) The method of claim 1, wherein the framework has the formula:



in which:

R₁ is 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl;

F₁ and F₂ are independently carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group; or are independently 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted

heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group;

F₃ and F₄ are independently absent, carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group; or are independently absent, or 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group.

73. (Previously presented) The method of claim 72, wherein:

R₁ is 1-6 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl;

F₁, F₂, F₃, or F₄ are independently 1-6 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group.

F₃ is absent; or

F₃ and F₄ are absent.

74. (Currently amended) The method of claim 1, wherein the framework is:
a natural or synthetic amino acid, an α -hydroxy acid, or a thioic acid; or
a β -amino acid[[s]] or homo or β analog of a natural amino acid.

75. (Previously presented) The method of claim 1, wherein the framework is an amino acid with an amine, hydroxyl, phenol, carboxyl, thiol, thioether, or amidino group on its side chain.

76. (Previously presented) The method of claim 1, wherein the framework is a serine, threonine, tyrosine, aspartic acid, glutamic acid, asparagine, glutamine, cysteine, lysine, arginine, or histidine moiety.

77-78. (Canceled)

79. (Currently amended) The method of claim 8, wherein each recognition element is independently unsubstituted or substituted with a moiety selected from the group consisting of amine, quaternary ammonium, carboxylate, phenol, phosphate, phosphonate, phosphinate, sulphate, sulphonate, thiocarboxylate, hydroxamic acid, sulfoxide, betaine, amine oxide, amide, carboxyl, alcohol, ether, thiol, thioether, ester, thio ester, borane, borate, metal complex, alkyl, alkene, alkyne, aromatic moiety, and plurality thereof.

80. (Previously presented) The method of claim 8, wherein a recognition element is substituted with or to form:

protonated phosphate, protonated phosphonate, protonated phosphinate, protonated sulphate, or protonated sulphinate;

alkyl amine, alkyl diamine, heteroalkyl amine, aryl amine, heteroaryl amine, aryl alkyl amine, heterocyclic amine, amidine, hydrazine, urea, trimethyl alkyl quaternary ammonium, dimethyl ethyl alkyl quaternary ammonium, dimethyl alkyl quaternary ammonium, aryl alkyl quaternary ammonium, or pyridinium quaternary ammonium;

alkyl carboxylate, aryl carboxylate, aryl alkyl carboxylate, or thiocarboxylate;

phosphonate or phosphinate;

primary alcohol, secondary alcohol, tertiary alcohol, or aromatic alcohol;

lower alkyl, substituted alkyl, cycloalkyl, aryl alkyl, heteroaryl alkyl, lower alkene, aryl alkene, unsubstituted aryl, heteroaryl, substituted aryl, aryl alkyl, heteroaryl alkyl, alkyl substituted aryl, or polyaromatic hydrocarbon; or
a plurality thereof.

81. (Previously presented) The method of claim 8, wherein the framework has the formula:



in which:

R₁ is 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl;

F₁ and F₂ are independently carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group; or are independently 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group;

F₃ and F₄ are independently absent, carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group; or are independently absent, or 1-12 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group.

82. (Previously presented) The method of claim 81, wherein:

R₁ is 1-6 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, or heteroaryl alkyl;

F₁, F₂, F₃, or F₄ are independently 1-6 carbon alkyl, substituted alkyl, cycloalkyl, heterocyclic, substituted heterocyclic, aryl alkyl, aryl, heteroaryl, heteroaryl alkyl, or inorganic group substituted with carboxyl, amine, hydroxyl, phenol, carbonyl, or thiol group.

F₃ is absent; or

F₃ and F₄ are absent.

83. (Currently amended) The method of claim 8, wherein the framework is:
a natural or synthetic amino acid, an α -hydroxy acid, or a thioic acid; or
a β -amino acid[[s]] or homo or β analog of a natural amino acid.

84. (Previously presented) The method of claim 8, wherein the framework is an amino acid with an amine, hydroxyl, phenol, carboxyl, thiol, thioether, or amidino group on its side chain.

85. (Previously presented) The method of claim 8, wherein the framework is a serine, threonine, tyrosine, aspartic acid, glutamic acid, asparagine, glutamine, cysteine, lysine, arginine, or histidine moiety.

86-87. (Canceled)

88. (New) The method of claim 1, wherein independently reversibly immobilizing comprises coupling the building block to the solid support employing a readily reversible covalent bond; and the readily reversible covalent bond forms an imine, an acetal, a ketal, a disulfide, or an ester.

89. (New) The method of claim 8, wherein independently reversibly immobilizing comprises coupling the building block to the solid support employing a readily reversible covalent bond; and the readily reversible covalent bond forms an imine, an acetal, a ketal, a disulfide, or an ester.

90. (New) The method of claim 1, wherein the lawn of moieties that can engage in van der Waals interactions comprises a lawn of branched or straight chain C₆₋₃₆ alkyl, C₈₋₂₄ alkyl, C₁₂₋₂₄ alkyl, C₁₂₋₁₈ alkyl; C₆₋₃₆ alkenyl, C₈₋₂₄ alkenyl, C₁₂₋₂₄ alkenyl, C₁₂₋₁₈ alkenyl with 1 to 4 double bonds; C₆₋₃₆ alkynyl, C₈₋₂₄ alkynyl, C₁₂₋₂₄ alkynyl, or C₁₂₋₁₈ alkynyl with 1 to 4 triple bonds; or a mixture thereof.

91. (New) The method of claim 1, wherein the lawn of moieties that can engage in van der Waals interactions comprises a lawn of branched or straight chain C₆₋₃₆ alkyl, C₈₋₂₄ alkyl, C₁₂₋₂₄ alkyl, C₁₂₋₁₈ alkyl; C₆₋₃₆ alkenyl, C₈₋₂₄ alkenyl, C₁₂₋₂₄ alkenyl, C₁₂₋₁₈ alkenyl with 1 to 4 double bonds; C₆₋₃₆ alkynyl, C₈₋₂₄ alkynyl, C₁₂₋₂₄ alkynyl, or C₁₂₋₁₈ alkynyl with 1 to 4 triple bonds; or a mixture thereof.